

Naval Medical Center Portsmouth (NMCP) COVID-19 Literature Report

#92: Friday, 29 April 2022

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, special reports, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers. I welcome questions, suggestions for future topics, or other feedback. If this report made a difference or impacted patient care, please let me know!

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Due to the rapid evolution of the literature, I will not update past reports when new information arises; for retracted papers specific to COVID-19, see the [list of retracted papers from Retraction Watch](#).

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The Big Picture

News in Brief

"U.S. no longer in 'full-blown' pandemic phase, Fauci says" ([WP](#)).

"New CDC team: A 'Weather Service' to forecast what's next in pandemic" ([WP](#)).

"South Africa likely to see fifth COVID wave — Recent sharp increases in test positivity, cases driven by BA.4 and BA.5 variants" ([Medpage](#)).

"'Without a word for what we know': The unfathomable loss of a million U.S. Covid deaths" ([STAT](#)).

Preparedness

"[Resilient Drug Supply Project] maps medicine supply to US to predict, prevent shortages" ([CIDRAP part 2 of 2](#); previously: [part 1](#)).

"Four lessons from the pandemic to reboot the NIH" ([Nature](#)).

"CIDRAP to develop vaccine roadmap for future coronavirus threats" ([CIDRAP](#)).

Mis/Disinformation

"Their mom died of COVID. They say conspiracy theories are what really killed her" ([NPR](#)).

"Online misinformation is linked to early COVID-19 vaccination hesitancy and refusal" ([Sci Rep](#)).

Long Reads

"Covid hasn't given up all its secrets. Here are 6 mysteries experts hope to unravel" ([STAT](#)).

Military Matters

"The military might be creating 'a perfect storm' for eating disorders" ([NPR](#)).

Webinars and Events

WHAT: [What Happened to the Plans? Lessons Observed from COVID-19 - A Workshop](#)

WHEN: Tuesday, 17 May 2022 0900–1630 EDT
Wednesday, 18 May 2022 0900–1540 EDT

DETAILS: The National Academies of Sciences, Engineering, and Medicine will organize and convene a two-day in person public workshop where invited speakers will explore the nation's Public Health Emergency (PHE) preparedness & response enterprise through the lens the COVID-19 response in the United States.

The workshop will explore key components, success stories, as well as failure points throughout the entire PHE preparedness and response enterprise in order to identify opportunities for more effective catastrophic disaster, pandemic, and other large scale PHEs planning at the federal, state, local, tribal, and territorial levels. Specifically, the workshop will examine weaknesses and opportunities in the PHE's systems architecture, including but not limited to:

- Global disease surveillance;
- Medical Supply chain and Medical Counter Measure (MCM) viability and vulnerabilities;
- The continuum of local-state-regional-national coordination challenges and leadership incident command structure disparities,
- Preparedness and response capabilities, authorities, and funding streams; and
- Engaging with vulnerable populations, risk communication and messaging failures.

Special Reports and Other Resources

BCB: [The Athena Agenda: Advancing the Apollo Program for Biodefense](#) (April 2022)

"The Bipartisan Commission on Biodefense warned that the United States was woefully unprepared for biological threats and that the risk to the Nation was rising rapidly in our baseline 2015 report, *A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts*. A little over six years later, the US experience with COVID-19 and the proliferation of biological weapons programs² continue to validate our original findings.

Since we released *The Apollo Program for Biodefense: Winning the Race Against Biological Threats* in January 2021, the world has yet to surmount COVID-19. Nearly one million American deaths and more than \$16 trillion in US economic losses have made COVID-19 the deadliest pandemic in this country's history and the costliest domestic catastrophe since the Great Depression. This pandemic has killed over six million people around the world, ravaged health systems, destroyed economies, and exposed destabilizing divisions within and among countries. And yet, the Commission remains convinced that COVID-19 is not a once-in-a-century pandemic. Another biological event will occur much earlier than that.

The risk of naturally occurring pandemics grows as biodiversity is reducing due to deforestation and diminished wildlife habitat quality. The exploitation of wildlife through hunting and trade facilitates opportunities for animal-human interactions and zoonotic disease transmission. Furthermore, advances in DNA sequencing, gene-editing, and

synthetic biology (among others) hold the promise of profound advances in healthcare, crop and environmental sustainability, and economic growth. Unfortunately, these are dual-use technologies that could yield accidental, unintended, and deliberate misuse by creating deadly pathogens or disrupting ecological balances. Examples include the accidental release of smallpox from a laboratory in the United Kingdom, engineering of a deadly strain of influenza by a professor in the Netherlands, inadvertent self-injection of Ebola by an experienced scientist in Russia, and the unintended escape of Brucellosis from an industrial facility in China.

Our country must decide to make the prevention and deterrence of the next biological incident top priorities. We cannot simply afford to focus on the response to the current pandemic, but must work to put in place mitigation measures to reduce the impact of future biological events. Continuing vulnerabilities revealed by biological threats increase the likelihood that our enemies will attack our country with biological weapons, especially as advances in science and technology make it easier to produce such weapons.

Throughout our country's history, our government has risen to seemingly impossible challenges by pursuing grand programs. It was hard to imagine landing a person on the Moon in 1961 when President John F. Kennedy committed the United States to achieving that goal in 10 years. Our country accomplished the Apollo 11 mission 9 years later, with 161 days to spare. The United States can similarly put an end to pandemics within a decade.

The Athena Agenda: Advancing The Apollo Program for Biodefense contains additional recommendations to execute The Apollo Program, building on the Commission's previous work and taking into consideration the efforts of current and former Administrations and Congresses. This report provides the following specific governance and technology recommendations to implement The Apollo Program for Biodefense and identifies the US government organizations responsible for leadership and accountability, though certain actions may require or benefit from public-private partnerships."

Journal Articles

MMWR: [Provisional COVID-19 Age-Adjusted Death Rates, by Race and Ethnicity — United States, 2020–2021](#) (29 April 2022)

BLUF: COVID was the third leading cause of US deaths in 2021 and we still have a lot of racial and ethnic disparities.

"What is already known about this topic? In 2020, racial and ethnic disparities in COVID-19 age-adjusted death rates (AADR) were reported among U.S. residents.

What is added by this report? From 2020 to 2021, disparities in AADR ratios from COVID-19 decreased significantly by 14.0%–40.2% for most racial and ethnic groups, including non-Hispanic White persons, who accounted for 59.6%–65.2% of all decedents; and increased nonsignificantly (7.2%) for non-Hispanic Native Hawaiian and other Pacific Islander persons (0.2%–0.3% of all decedents) compared with non-Hispanic multiracial persons.

What are the implications for public health practice? Providing effective preventive interventions, including vaccination and clinical care, to all communities in proportion to their need for these interventions is necessary to reduce racial and ethnic disparities in COVID-19 deaths."

Beyond COVID – Other Important Literature

Infect Control Hosp Epidemiol: [Strategies to prevent central line-associated bloodstream infections in acute-care hospitals: 2022 Update](#) (19 April 2022)

"Previously published guidelines provide comprehensive recommendations for detecting and preventing healthcare-associated infections (HAIs). The intent of this document is to highlight practical recommendations in a concise format designed to assist acute-care hospitals in implementing and prioritizing their central line-associated bloodstream infection (CLABSI) prevention efforts. This document updates the Strategies to Prevent Central Line-Associated Bloodstream Infections in Acute-Care Hospitals published in 2014. This expert guidance document is sponsored by the Society for Healthcare Epidemiology of America (SHEA). It is the product of a collaborative effort led by SHEA, the Infectious Diseases Society of America (IDSA), the Association for Professionals in Infection Control and Epidemiology (APIC), the American Hospital Association (AHA), and The Joint Commission, with major contributions from representatives of a number of organizations and societies with content expertise."

SARS-CoV-2 Virus and Variants

News in Brief

"Introducing SARS-CoV-2 Variants Overview, NLM's latest tool in the fight against COVID-19" ([NLM](#); see also: [online dashboard](#)).

"Are new Omicron subvariants a threat? Here's how scientists are keeping watch" ([Nature](#)).

"Omicron splinters into fast-spreading lineages, highlighting coronavirus's evolution" ([STAT](#)).

"BA.2.12.1 subvariant: concerning, but no need to panic just yet — A number of factors are contributing to the Omicron subvariant's rise" ([Medpage](#)).

Clinical Impact

"Omicron infection just 20 days after Delta – the shortest known gap between infections: Fully vaccinated and boosted 31-year-old woman tested positive for Omicron strain of SARS-CoV-2 just 20 days after having Delta infection" ([EurekAlert](#)).

Zoonotic

"COVID is spreading in deer. What does that mean for the pandemic?" ([Nature](#))

"4 Michiganders with COVID-19 strain unique to mink were likely 1st US spillover cases" ([DFP](#)).

Journal Articles

Lancet Infect Dis: [Severity of omicron variant of concern and effectiveness of vaccine boosters against symptomatic disease in Scotland \(EAVE II\): a national cohort study with nested test-negative design](#) (22 April 2022)

"Background: Since its emergence in November, 2021, in southern Africa, the SARS-CoV-2 omicron variant of concern (VOC) has rapidly spread across the world. We aimed to investigate the severity of omicron and the extent to which booster vaccines are effective in preventing symptomatic infection.

Methods: In this study, using the Scotland-wide Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II) platform, we did a cohort analysis with a nested test-negative design incident case-control study covering the period Nov 1-Dec 19, 2021, to provide initial estimates of omicron severity and the effectiveness of vaccine boosters against symptomatic disease relative to 25 weeks or more after the second vaccine dose. Primary care data derived from 940 general practices across Scotland were linked to laboratory data and hospital admission data. We compared outcomes between infection with the delta VOC (defined as S-gene positive) and the omicron VOC (defined as S-gene negative). We assessed effectiveness against symptomatic SARS-CoV-2 infection, with infection confirmed through a positive RT-PCR.

Findings: By Dec 19, 2021, there were 23 840 S-gene-negative cases in Scotland, which were predominantly among those aged 20-39 years (11 732 [49.2%]). The proportion of S-gene-negative cases that were possible reinfections was more than ten times that of S-gene-positive cases (7.6% vs 0.7%; $p < 0.0001$). There were 15 hospital admissions in S-gene-negative individuals, giving an adjusted observed-to-expected admissions ratio of 0.32 (95% CI 0.19-0.52). The booster vaccine dose was associated with a 57% (54-60) reduction in the

risk of symptomatic S-gene-negative infection relative to individuals who tested positive 25 weeks or more after the second vaccine dose.

Interpretation: These early national data suggest that omicron is associated with a two-thirds reduction in the risk of COVID-19 hospitalisation compared with delta. Although offering the greatest protection against delta, the booster dose of vaccination offers substantial additional protection against the risk of symptomatic COVID-19 for omicron compared with 25 weeks or more after the second vaccine dose."

Cold Spring Harb Perspect Med: [The Evolution and Biology of SARS-CoV-2 Variants](#) (20 April 2022)

"Our understanding of the still unfolding severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic would have been extremely limited without the study of the genetics and evolution of this new human coronavirus. Large-scale genome-sequencing efforts have provided close to real-time tracking of the global spread and diversification of SARS-CoV-2 since its entry into the human population in late 2019. These data have underpinned analysis of its origins, epidemiology, and adaptations to the human population: principally immune evasion and increasing transmissibility. SARS-CoV-2, despite being a new human pathogen, was highly capable of human-to-human transmission. During its rapid spread in humans, SARS-CoV-2 has evolved independent new forms, the so-called "variants of concern," that are better optimized for human-to-human transmission. The most important adaptation of the bat coronavirus progenitor of both SARS-CoV-1 and SARS-CoV-2 for human infection (and other mammals) is the use of the angiotensin-converting enzyme 2 (ACE2) receptor. Relaxed structural constraints provide plasticity to SARS-related coronavirus spike protein permitting it to accommodate significant amino acid replacements of antigenic consequence without compromising the ability to bind to ACE2. Although the bulk of research has justifiably concentrated on the viral spike protein as the main determinant of antigenic evolution and changes in transmissibility, there is accumulating evidence for the contribution of other regions of the viral proteome to virus-host interaction. Whereas levels of community transmission of recombinants compromising genetically distinct variants are at present low, when divergent variants cocirculate, recombination between SARS-CoV-2 clades is being detected, increasing the risk that viruses with new properties emerge. Applying computational and machine learning methods to genome sequence data sets to generate experimentally verifiable predictions will serve as an early warning system for novel variant surveillance and will be important in future vaccine planning. Omicron, the latest SARS-CoV-2 variant of concern, has focused attention on step change antigenic events, "shift," as opposed to incremental "drift" changes in antigenicity. Both an increase in transmissibility and antigenic shift in Omicron led to it readily causing infections in the fully vaccinated and/or previously infected. Omicron's virulence, while reduced relative to the variant of concern it replaced, Delta, is

very much premised on the past immune exposure of individuals with a clear signal that boosted vaccination protects from severe disease. Currently, SARS-CoV-2 has proven itself to be a dangerous new human respiratory pathogen with an unpredictable evolutionary capacity, leading to a risk of future variants too great not to ensure all regions of the world are screened by viral genome sequencing, protected through available and affordable vaccines, and have non-punitive strategies in place for detecting and responding to novel variants of concern."

EBioMedicine: [The displacement of the SARS-CoV-2 variant Delta with Omicron: An investigation of hospital admissions and upper respiratory viral loads](#) (20 April 2022)

"Background: The increase in SARS-CoV-2 infections in December 2021 was driven primarily by the Omicron variant, which largely displaced the Delta over a three-week span. Outcomes from infection with Omicron remain uncertain. We evaluated whether clinical outcomes and viral loads differed between Delta and Omicron infections during the period when both variants were co-circulating.

Methods: In this retrospective observational cohort study, remnant clinical specimens, positive for SARS-CoV-2 after standard of care testing at the Johns Hopkins Microbiology Laboratory, between the last week of November and the end of December 2021, were used for whole viral genome sequencing. Cycle threshold values (Ct) for viral RNA, the presence of infectious virus, and levels of respiratory IgG were measured, and clinical outcomes were obtained. Differences in each measure were compared between variants stratified by vaccination status.

Findings: The Omicron variant displaced Delta during the study period and constituted 95% of the circulating lineages by the end of December 2021. Patients with Omicron infections (N = 1,119) were more likely to be vaccinated compared to patients with Delta (N = 908), but were less likely to be admitted (0.33 CI 0.21-0.52), require ICU level care (0.38 CI 0.17-0.87), or succumb to infection (0.26 CI 0.06-1.02) regardless of vaccination status. There was no statistically significant difference in Ct values based on the lineage regardless of the vaccination status. Recovery of infectious virus in cell culture was reduced in boosted patients compared to fully vaccinated without a booster and unvaccinated when infected with the Delta lineage. However, in patients with Omicron infections, recovery of infectious virus was not affected by vaccination.

Interpretation: Compared to Delta, Omicron was more likely to cause breakthrough infections of vaccinated individuals, yet admissions were less frequent. Admitted patients might develop severe disease comparable to Delta. Efforts for reducing Omicron transmission are required as, though the admission risk might be lower, the increased numbers of infections cause large numbers of hospitalizations."

Transmission, Exposure, and Surveillance

News in Brief

"Better ventilation can prevent covid spread. But are companies paying attention?" ([KHN](#)).

At least 90 high school students tested positive for COVID-19 after a mask-optional prom in San Francisco ([ABC](#)).

"WHO chief says we are 'increasingly blind' on COVID transmission" ([Reuters](#)).

"EU estimates up to 80% of population has had COVID" ([Reuters](#)).

Journal Articles

MMWR: [Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies — United States, September 2021–February 2022](#) (29 April 2022)

"This report uses data from CDC's national commercial laboratory seroprevalence study and the 2018 American Community Survey to examine U.S. trends in infection-induced SARS-CoV-2 seroprevalence during September 2021–February 2022, by age group.

As of February 2022, approximately 75% of children and adolescents had serologic evidence of previous infection with SARS-CoV-2, with approximately one third becoming newly seropositive since December 2021. The greatest increases in seroprevalence during September 2021–February 2022, occurred in the age groups with the lowest vaccination coverage; the proportion of the U.S. population fully vaccinated by April 2022 increased with age (5–11, 28%; 12–17, 59%; 18–49, 69%; 50–64, 80%; and ≥65 years, 90%). Lower seroprevalence among adults aged ≥65 years, who are at greater risk for severe illness from COVID-19, might also be related to the increased use of additional precautions with increasing age.

These findings illustrate a high infection rate for the Omicron variant, especially among children."

Clin Infect Dis: [Airflow patterns in double occupancy patient rooms may contribute to roommate-to-roommate transmission of severe acute respiratory syndrome coronavirus 2](#) (27 April 2022)

"Background: Hospitalized patients are at risk to acquire severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from roommates with unrecognized coronavirus disease 2019 (COVID-19). We hypothesized that airflow patterns might contribute to SARS-CoV-2 transmission in double occupancy patient rooms.

Methods: A device emitting condensed moisture was used to identify airflow patterns in double occupancy patient rooms. Simulations were conducted to assess transfer of fluorescent microspheres, 5% sodium chloride aerosol, and aerosolized bacteriophage MS2 between patient beds 3 meters apart and to assess the effectiveness of privacy curtains and portable air cleaners in reducing transfer.

Results: Air flowed from inlet vents in the center of the room to an outlet vent near the door, resulting in air currents flowing toward the bed adjacent to the outlet vent. Fluorescent microspheres (212-250 μm diameter), 5% sodium chloride aerosol, and aerosolized bacteriophage MS2 released from the inner bed were carried on air currents toward the bed adjacent to the outlet vent. Closing curtains between the patient beds reduced transfer of each of the particles. Operation of a portable air cleaner reduced aerosol transfer to the bed adjacent to the outlet vent but did not offer a benefit over closing the curtains alone, and in some situations resulted in an increase in aerosol exposure.

Conclusion: Airflow patterns in double occupancy patient rooms may contribute to risk for transmission of SARS-CoV-2 between roommates. Keeping curtains closed between beds may be beneficial in reducing risk."

Emerg Infect Dis: [Estimating Relative Abundance of 2 SARS-CoV-2 Variants through Wastewater Surveillance at 2 Large Metropolitan Sites, United States](#) (19 April 2022)

"Monitoring severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern (VOCs) is critical for public health management of coronavirus disease. Sequencing is resource-intensive and incompletely representative, and not all isolates can be sequenced. Because wastewater SARS-CoV-2 RNA concentrations correlate with coronavirus disease incidence in sewersheds, tracking VOCs through wastewater is appealing. We developed digital reverse transcription PCRs to monitor abundance of select mutations in Alpha and Delta VOCs in wastewater settled solids, applied these to July 2020–August 2021 samples from 2 large US metropolitan sewersheds, and compared results to estimates of VOC abundance from case isolate sequencing. Wastewater measurements tracked closely with case isolate estimates (Alpha, r_p 0.82–0.88; Delta, r_p 0.97). Mutations were detected in wastewater even at levels <5% of total SARS-CoV-2 RNA and in samples available 1–3 weeks before case isolate results. Wastewater variant monitoring should be strategically deployed to complement case isolate sequencing."

COVID-19 Vaccines

News in Brief

"Moderna: bivalent COVID booster passes muster" ([Medpage](#)).

"Longer COVID vaccine dose interval tied to higher antibody levels" ([CIDRAP](#); see also: [ESCMID preprint \[pdf\]](#)).

"Experts fear U.S. may default to annual Covid boosters without sufficient data" ([STAT](#)).

"Denmark becomes the first country to halt its Covid vaccination program" ([CNBC](#)).

Journal Articles

Clin Infect Dis: [Effectiveness of mRNA-based vaccines during the emergence of SARS-CoV-2 Omicron variant](#) (27 April 2022)

"Background: We evaluated effectiveness of mRNA-based vaccines following emergence of SARS-CoV-2 Omicron variant.

Methods: Recipients of a third dose of BNT162b2 or mRNA-1273 ≥ 180 days after the primary series were matched to primary series recipients and unvaccinated persons. Participants were followed from December 1, 2021 to March 12, 2022. Outcomes were documented SARS-CoV-2 infection, COVID-19 hospitalization, and COVID-19 death. Effectiveness was calculated from 100-day risks estimated with the Kaplan-Meier estimator.

Results: BNT162b2 and mRNA-1273 groups respectively included 221,267 and 187,507 third dose recipients matched to equal numbers of primary series recipients and unvaccinated persons. Compared to no vaccination, effectiveness of a third dose of BNT162b2 was 47.8% (95% confidence interval [CI]: 45.2-50.3), 81.8% (95% CI 79.2-84.2), and 89.6% (95% CI 85.0-93.6) against documented infection, hospitalization, and death, respectively. Effectiveness of a third dose of BNT162b2 compared to the primary series was 30.1% (95% CI 26.2-33.7), 61.4% (95% CI 55.0-67.1), and 78.8% (95% CI 67.9-87.5) against documented infection, hospitalization, and death, respectively. Effectiveness of a third dose of mRNA-1273 compared to no vaccination was 61.9% (95% CI 59.4-64.4), 87.9% (95% CI 85.3-90.2), and 91.4% (95% CI 86.4-95.6) against documented infection, hospitalization, and death, respectively. Effectiveness of a third dose of mRNA-1273 compared to the primary series was 37.1% (95% CI 32.2-41.7), 63.5% (95% CI 53.7-71.6), and 75.0% (95% CI 55.4-88.0) against documented infection, hospitalization, and death, respectively.

Conclusions: BNT162b2 and mRNA-1273 were effective against COVID-19 following emergence of Omicron variant. A third dose provided additional protection over the primary series."

Nat Med: [Effectiveness of a second BNT162b2 booster vaccine against hospitalization and death from COVID-19 in adults aged over 60 years](#) (25 April 2022)

"The rapid emergence of the B.1.1.529 (Omicron) variant of SARS-CoV-2 led to a global resurgence of coronavirus disease 2019 (COVID-19). Israeli authorities approved a fourth COVID-19 vaccine dose (second-booster) for individuals aged 60 years and over who had received a first booster dose four or more months earlier. Evidence regarding the effectiveness of a second-booster dose in reducing hospitalizations and mortality due to COVID-19 is warranted. This retrospective cohort study included all members of Clalit Health Services, aged 60 to 100 years, who were eligible for the second-booster on January 3, 2022. Hospitalizations and mortality due to COVID-19 among participants who received the second-booster were compared with participants who received one booster dose. Cox proportional-hazards regression models with time-dependent covariates were used to estimate the association between the second-booster and hospitalizations and death due to COVID-19 while adjusting for demographic factors and coexisting illnesses. A total of 563,465 participants met the eligibility criteria. Of those, 328,597 (58%) received a second-booster dose during the 40-day study period. Hospitalizations due to COVID-19 occurred in 270 of the second-booster recipients and in 550 participants who received one booster dose (adjusted hazard ratio 0.36; 95% confidence interval (CI): 0.31 to 0.43). Death due to COVID-19 occurred in 92 second-booster recipients and in 232 participants who received one booster dose (adjusted hazard ratio 0.22; 95% CI 0.17 to 0.28). This study demonstrates a substantial reduction in hospitalizations and deaths due to Covid-19 conferred by a second-booster in Israeli adults aged 60 years and over."

JAMA Netw Open: [Assessment of T-cell Reactivity to the SARS-CoV-2 Omicron Variant by Immunized Individuals](#) (22 April 2022)

"Question: What is the cellular immunity associated with the Omicron variant of SARS-CoV-2 among immunized individuals?

Findings: In this cohort study among 61 individuals who had been vaccinated against COVID-19, cellular responses to the mutated regions of the Omicron spike protein were detected in 80% of participants. The mutations were associated with significantly reduced T-cell recognition compared with the vaccine strain, while reactivity to the whole spike protein was present in 100% of participants, and the proportion of remaining immunity to SARS-CoV-2 was estimated to be 87%.

Meaning: These findings suggest that cellular immunity to the Omicron variant was maintained despite the mutations in its spike protein; thus, immunization may confer protection from severe COVID-19 from the Omicron variant."

Nature: [Increased Memory B Cell Potency and Breadth After a SARS-CoV-2 mRNA Boost](#) (21 April 2022)

"The omicron variant of SARS-CoV-2 infected many vaccinated and convalescent individuals. Despite the reduced protection from infection, individuals that received 3 doses of an mRNA vaccine were highly protected from more serious consequences of infection. Here we examine the memory B cell repertoire in a longitudinal cohort of individuals receiving 3 mRNA vaccine doses. We find that the 3rd dose is accompanied by an increase in, and evolution of, anti-receptor binding domain-specific memory B cells. The increase is due to expansion of memory B cell clones that were present after the 2nd dose as well as the emergence of new clones. The antibodies encoded by these cells showed significantly increased potency and breadth when compared to antibodies obtained after the 2nd dose. Notably, the increase in potency was especially evident among newly developing clones of memory cells that differed from the persisting clones in targeting more conserved regions of the RBD. Overall, more than 50% of the analyzed neutralizing antibodies in the memory compartment after a 3rd mRNA vaccine dose neutralized Omicron. Thus, individuals receiving 3 doses of an mRNA vaccine, have a diverse memory B cell repertoire that can respond rapidly and produce antibodies capable of clearing even diversified variants such as Omicron. These data help explain why a 3rd dose of a vaccine that was not specifically designed to protect against variants is effective against variant-induced serious disease."

JAMA Netw Open: [Effectiveness of mRNA-1273, BNT162b2, and JNJ-78436735 COVID-19 Vaccines Among US Military Personnel Before and During the Predominance of the Delta Variant](#) (20 April 2022)

"Question: Did the effectiveness of the mRNA-1273, BNT162b2, and JNJ-78436735 COVID-19 vaccines change among US-based military personnel before and during the predominance of the SARS-CoV-2 Delta (B.1.617.2) variant?

Findings: In this case-control study of 441 379 active US military personnel, overall COVID-19 vaccine effectiveness decreased by 19% from the pre-Delta to the Delta period. JNJ-78436735 had the lowest overall vaccine effectiveness in the pre-Delta (81.8%) and Delta (38.3%) periods.

Meaning: In this study, COVID-19 vaccine effectiveness decreased among US-based military personnel during the time of SARS-CoV-2 Delta variant predominance, especially for recipients of the JNJ-78436735 vaccine; this finding supports the use of booster doses to increase effectiveness."

Adverse Events

Emerg Infect Dis: [Type 1 Diabetes Mellitus Associated with Nivolumab after Second SARS-CoV-2 Vaccination, Japan](#) (25 April 2022)

"Recently, along with increasing use of immune checkpoint inhibitors such as nivolumab, the incidence of immune-related adverse events, including type 1 diabetes mellitus, has become a serious problem. We report a patient who had immune checkpoint inhibitor-associated type 1 diabetes mellitus that developed after a second mRNA-based SARS-CoV-2 vaccination."

JAMA Cardiol: [SARS-CoV-2 Vaccination and Myocarditis in a Nordic Cohort Study of 23 Million Residents](#) (20 April 2022)

"Question: Is SARS-CoV-2 messenger RNA (mRNA) vaccination associated with risk of myocarditis?

Findings: In a cohort study of 23.1 million residents across 4 Nordic countries, risk of myocarditis after the first and second doses of SARS-CoV-2 mRNA vaccines was highest in young males aged 16 to 24 years after the second dose. For young males receiving 2 doses of the same vaccine, data were compatible with between 4 and 7 excess events in 28 days per 100 000 vaccinees after second-dose BNT162b2, and between 9 and 28 per 100 000 vaccinees after second-dose mRNA-1273.

Meaning: The risk of myocarditis in this large cohort study was highest in young males after the second SARS-CoV-2 vaccine dose, and this risk should be balanced against the benefits of protecting against severe COVID-19 disease."

Breakthrough Infections, Reinfections, and Coinfections

Journal Articles

Clin Infect Dis: [Coronavirus Disease 2019 \(COVID-19\) Vaccine Boosting in Previously Infected or Vaccinated Individuals](#) (27 April 2022)

"Background: The purpose of this study was to evaluate whether boosting previously infected or vaccinated healthcare personnel with a vaccine developed for an earlier variant of SARS-CoV-2 protects against the Omicron variant.

Methods: Employees of Cleveland Clinic previously infected with or vaccinated against COVID-19, and working in Ohio the day the Omicron variant was declared a variant of concern, were included. The cumulative incidence of COVID-19 was examined over two

months during an Omicron variant surge. Protection provided by boosting (analyzed as a time-dependent covariate) was evaluated using Cox proportional hazards regression. Analyses were adjusted for time since proximate SARS-CoV-2 exposure as a time-dependent covariate.

Results: Among 39 766 employees, 8037 (20%) previously infected and the remaining previously vaccinated, COVID-19 occurred in 6230 (16%) during the study. Risk of COVID-19 increased with time since proximate SARS-CoV-2 exposure, and boosting protected those >6 months since prior infection or vaccination. In multivariable analysis, boosting was independently associated with lower risk of COVID-19 among those vaccinated but not previously infected (HR, .43; 95% CI, .41-.46) as well as those previously infected (HR, .66; 95% CI, .58-.76). Among those previously infected, receiving 2 compared to 1 dose of vaccine was associated with higher risk of COVID-19 (HR, 1.54; 95% CI, 1.21-1.97).

Conclusions: Administering a COVID-19 vaccine not designed for the Omicron variant, >6 months after prior infection or vaccination, protects against Omicron variant infection in those previously infected or vaccinated. There is no evidence of an advantage to administering more than 1 dose of vaccine to previously infected persons."

Infect Dis Ther: [Patients with COVID-19 and HBV Coinfection are at Risk of Poor Prognosis](#) (26 April 2022)

"Introduction: This study aimed to determine whether there is a difference in the risk of death/critical illness between different stages of hepatitis B virus (HBV) (resolved hepatitis B, HBeAg (-) chronic hepatitis B [CHB]/infection, HBeAg (+) CHB/infection, and HBV reactivation) coinfecting with coronavirus disease 2019 (COVID-19); and if there is a difference, whether it is due to abnormal liver function and to what extent.

Methods: This cohort study included all COVID-19 inpatients of a single-center tertiary care academic hospital in Wuhan, Hubei, China, between February 4, 2020, and follow-up to April 14, 2020. A total of 2899 patients with COVID-19 were included as participants in this study, and they were divided into five groups based on hepatitis B infection status. Follow-up was conducted for mortality and ICU admission during hospitalization.

Results: The median follow-up time was 39 days (IQR, 30-50), with 66 deaths and 126 ICU admissions. After adjustment, compared with patients without CHB, the hazard ratio (HR) for ICU admission was 1.86 (95% CI: 1.05-3.31) for patients with HBeAg (+) CHB/infection. The HR for death was 3.19 (95% CI: 1.62-6.25) for patients with HBeAg (+) CHB/infection. The results for the mediating effect indicated that the total effect of HBeAg (+) CHB/infection on death/ICU stay was partially mediated by abnormal liver function, which accounted for 79.60% and 73.53%, respectively.

Conclusion: Patients with COVID-19 coinfecting with HBV at the HBeAg (+) CHB/infection stage have an increased risk of poor prognosis, and abnormal liver function partially mediates this increased risk of poor prognosis caused by the coinfection."

J Infect Dis: [Breakthrough gastrointestinal COVID and intra-host evolution consequent to combination monoclonal antibody prophylaxis](#) (16 April 2022)

"Breakthrough gastrointestinal COVID was observed after experimental SARS-CoV-2 upper mucosal infection in a rhesus macaque undergoing low-dose monoclonal antibody prophylaxis. High levels of viral RNA were detected in intestinal sites contrasting with minimal viral replication in upper respiratory mucosa. Sequencing of virus recovered from tissue in three gastrointestinal sites and rectal swab revealed loss of furin cleavage site deletions present in the inoculating virus stock and two amino acid changes in spike that were detected in two colon sites but not elsewhere, suggesting compartmentalized replication and intestinal viral evolution. This suggests suboptimal antiviral therapies promote viral sequestration in these anatomies."

Treatments and Management

News in Brief

CDC Health Advisory: "Updated Information on Availability and Use of Treatments for Outpatients with Mild to Moderate COVID-19 Who are at Increased Risk for Severe Outcomes of COVID-19" ([CDC \[pdf\]](#)).

"A puzzling phenomenon: Patients report a rebound of COVID-19 symptoms after taking the antiviral Paxlovid" ([Boston Globe](#)).

"Patients hospitalized with COVID-19 were three times as likely to die than those with seasonal influenza: Spanish study conducted during first pandemic wave finds adults hospitalised with COVID-19 were three times as likely to die within 30 days and 90 days than those hospitalised for seasonal influenza" ([EurekAlert](#); see also: [ECCMID abstract \[google drive pdf\]](#)).

"WHO recommends Paxlovid as treatment for high risk COVID-19 patients, but warns of roadblocks" ([HPN](#)).

"Why cheap, older drugs that might treat covid never get out of the lab" ([KHNN](#)).

Journal Articles

Clin Infect Dis: [Favipiravir for treatment of outpatients with asymptomatic or uncomplicated COVID-19: a double-blind randomized, placebo-controlled, phase 2 trial](#) (21 April 2022)

"Background: Favipiravir is an oral, RNA-dependent RNA polymerase inhibitor with in vitro activity against SARS-CoV2. Despite limited data, favipiravir is administered to patients with COVID-19 in several countries.

Methods: We conducted a phase 2 double-blind randomized controlled outpatient trial of favipiravir in asymptomatic or mildly symptomatic adults with a positive SARS-CoV2 RT-PCR within 72 hours of enrollment. Participants were randomized 1: 1 to receive placebo or favipiravir (1800mg BID Day 1, 800 mg BID Days 2-10). The primary outcome was SARS-CoV-2 shedding cessation in a modified intention-to-treat (mITT) cohort of participants with positive enrollment RT-PCRs. Using SARS-CoV-2 amplicon-based sequencing, we assessed favipiravir's impact on mutagenesis.

Results: From July 8, 2020 - March 23, 2021, we randomized 149 participants with 116 included in the mITT cohort. The participants' mean age was 43 years (SD 12.5) and 57 (49%) were women. We found no difference in time to shedding cessation by treatment arm overall (HR 0.76 favoring placebo, 95% confidence interval [CI] 0.48-1.20) or in subgroup analyses (age, sex, high-risk comorbidities, seropositivity or symptom duration at enrollment). We observed no difference in time to symptom resolution (initial: HR 0.84, 95% CI 0.54-1.29; sustained: HR 0.87, 95% CI 0.52-1.45). We detected no difference in accumulation of transition mutations in the viral genome during treatment.

Conclusions: Our data do not support favipiravir use at commonly used doses in outpatients with uncomplicated COVID-19. Further research is needed to ascertain if higher doses of favipiravir are effective and safe for patients with COVID-19."

Clin Infect Dis: [Comparison of hospitalized COVID-19 and influenza patients requiring supplemental oxygen in a cohort study: clinical impact and resource consumption](#) (20 April 2022)

"Background: To compare clinical characteristics, outcomes, and resource consumption of patients with COVID-19 and seasonal influenza requiring supplemental oxygen.

Methods: Retrospective cohort study conducted at a tertiary-care hospital. Patients admitted due to seasonal influenza between 2017 and 2019, or with COVID-19 between March and May 2020 requiring supplemental oxygen were compared. Primary outcome: 30-day mortality. Secondary outcomes: 90-day mortality and hospitalization costs. Attempted sample size to detect an 11% difference in mortality was 187 patients per group.

Results: COVID-19 cases were younger (median years, 67 (IQR 54-78) vs 76 (IQR 64-83); $p < 0.001$) and more frequently overweight whereas influenza cases had more hypertension, immunosuppression, and chronic heart, respiratory and renal disease. Compared to influenza, COVID-19 cases had more pneumonia (98% vs 60%, <0.001), higher MEWS and CURB-65 scores and were more likely to show worse progression on the WHO ordinal scale (33% vs 4%; $p < 0.001$). The 30-day mortality rate was higher for COVID-19 than for influenza: 15% vs 5% ($p = 0.001$). The median age of non-surviving cases was 81 (IQR 74-88) and 77.5 (IQR 65-84) ($p = 0.385$), respectively. COVID-19 was independently associated with 30-day (HR 4.6, 95%CI, 2-10.4) and 90-day (HR 5.2, 95%CI, 2.4-11.4) mortality. Sensitivity and subgroup analyses, including a subgroup considering only patients with pneumonia, did not show different trends. Regarding resource consumption, COVID-19 patients had longer hospital stays and higher critical care, pharmacy, and complementary test costs.

Conclusions: Although influenza patients were older and had more comorbidities, COVID-19 cases requiring supplemental oxygen on admission had worse clinical and economic outcomes."

NEJM: [Intramuscular AZD7442 \(Tixagevimab–Cilgavimab\) for Prevention of Covid-19](#) (20 April 2022)

"Background: The monoclonal-antibody combination AZD7442 is composed of tixagevimab and cilgavimab, two neutralizing antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that have an extended half-life and have been shown to have prophylactic and therapeutic effects in animal models. Pharmacokinetic data in humans indicate that AZD7442 has an extended half-life of approximately 90 days.

Methods: In an ongoing phase 3 trial, we enrolled adults (≥ 18 years of age) who had an increased risk of an inadequate response to vaccination against coronavirus disease 2019 (Covid-19), an increased risk of exposure to SARS-CoV-2, or both. Participants were randomly assigned in a 2:1 ratio to receive a single dose (two consecutive intramuscular injections, one containing tixagevimab and the other containing cilgavimab) of either 300 mg of AZD7442 or saline placebo, and they were followed for up to 183 days in the primary analysis. The primary safety end point was the incidence of adverse events after a single dose of AZD7442. The primary efficacy end point was symptomatic Covid-19 (SARS-CoV-2 infection confirmed by means of reverse-transcriptase-polymerase-chain-reaction assay) occurring after administration of AZD7442 or placebo and on or before day 183.

Results: A total of 5197 participants underwent randomization and received one dose of AZD7442 or placebo (3460 in the AZD7442 group and 1737 in the placebo group). The primary analysis was conducted after 30% of the participants had become aware of their randomized assignment. In total, 1221 of 3461 participants (35.3%) in the AZD7442 group and 593 of 1736 participants (34.2%) in the placebo group reported having at least one

adverse event, most of which were mild or moderate in severity. Symptomatic Covid-19 occurred in 8 of 3441 participants (0.2%) in the AZD7442 group and in 17 of 1731 participants (1.0%) in the placebo group (relative risk reduction, 76.7%; 95% confidence interval [CI], 46.0 to 90.0; $P < 0.001$); extended follow-up at a median of 6 months showed a relative risk reduction of 82.8% (95% CI, 65.8 to 91.4). Five cases of severe or critical Covid-19 and two Covid-19-related deaths occurred, all in the placebo group.

Conclusions: A single dose of AZD7442 had efficacy for the prevention of Covid-19, without evident safety concerns."

JAMA Intern Med: [Assessment of Awake Prone Positioning in Hospitalized Adults With COVID-19: A Nonrandomized Controlled Trial](#) (18 April 2022)

"Question: Is prone positioning associated with improved outcomes among patients with COVID-19 and hypoxemia requiring supplemental oxygen but not yet receiving mechanical ventilation?

Findings: In this nonrandomized controlled trial including 501 patients with COVID-19 and hypoxemia, the odds of having a worse outcome on study day 5 based on a modified World Health Organization ordinal scale was higher among patients receiving the awake prone positioning intervention.

Meaning: This study's findings suggest that routine recommendation for awake prone positioning among patients with COVID-19–related hypoxemia who require supplemental oxygen but not mechanical ventilation is not beneficial."

PLoS One: [Effect of common maintenance drugs on the risk and severity of COVID-19 in elderly patients](#) (18 April 2022)

"Background: Maintenance drugs are used to treat chronic conditions. Several classes of maintenance drugs have attracted attention because of their potential to affect susceptibility to and severity of COVID-19.

Methods: Using claims data on 20% random sample of Part D Medicare enrollees from April to December 2020, we identified patients diagnosed with COVID-19. Using a nested case-control design, non-COVID-19 controls were identified by 1:5 matching on age, race, sex, dual-eligibility status, and geographical region. We identified usage of angiotensin-converting enzyme inhibitors (ACEI), angiotensin-receptor blockers (ARB), statins, warfarin, direct factor Xa inhibitors, P2Y12 inhibitors, famotidine and hydroxychloroquine based on Medicare prescription claims data. Using extended Cox regression models with time-varying propensity score adjustment we examined the independent effect of each study drug on contracting COVID-19. For severity of COVID-19, we performed extended Cox regressions on all COVID-19 patients, using COVID-19-related hospitalization and all-cause mortality as outcomes. Covariates included gender, age, race, geographic region, low-income indicator,

and co-morbidities. To compensate for indication bias related to the use of hydroxychloroquine for the prophylaxis or treatment of COVID-19, we censored patients who only started on hydroxychloroquine in 2020.

Results: Up to December 2020, our sample contained 374,229 Medicare patients over 65 who were diagnosed with COVID-19. Among the COVID-19 patients, 278,912 (74.6%) were on at least one study drug. The three most common study drugs among COVID-19 patients were statins 187,374 (50.1%), ACEI 97,843 (26.2%) and ARB 83,290 (22.3%). For all three outcomes (diagnosis, hospitalization and death), current users of ACEI, ARB, statins, warfarin, direct factor Xa inhibitors and P2Y12 inhibitors were associated with reduced risks, compared to never users. Famotidine did not show consistent significant effects. Hydroxychloroquine did not show significant effects after censoring of recent starters.

Conclusion: Maintenance use of ACEI, ARB, warfarin, statins, direct factor Xa inhibitors and P2Y12 inhibitors was associated with reduction in risk of acquiring COVID-19 and dying from it."

Pre-Existing Conditions and Comorbidities

News in Brief

"UK patient had COVID-19 for 505 days straight, study shows" ([AP](#)).

Journal Articles

Clin Infect Dis: [The Impact of the SARS-CoV-2 Pandemic on Substance Use in the US](#) (27 April 2022)

"The SARS-CoV-2 pandemic has been associated with dramatic increases in substance use, as marked by increased alcohol, nicotine and cannabis sales. Lethal opioid overdoses also increased dramatically, especially during the initial phases of the epidemic when lockdowns and social isolation combined with increasing fentanyl contamination of the illicit drug supply resulted in more overdoses and fewer opportunities for rescue. Substance use, and especially inhalational drug use, increases the likelihood of both transmission and severe infection. Youth are especially vulnerable to substance use and have increased risk of long-term problems. These outcomes highlight the need for greater access to substance use treatment. Virtual treatment, which emerged as a promising format during the pandemic, may reduce access barriers. This manuscript reviews trends in substance use during the

pandemic, explores root causes of increased use and overdose and examines the potential to increase treatment through virtual care, especially during future periods of disruption."

Clin Infect Dis: [Cumulative Incidence and Risk Factors for Severe COVID-19 in French People with Cystic Fibrosis](#) (27 April 2022)

"Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections are closely monitored in people with cystic fibrosis (pwCF), with a special emphasis on severe cases. Previous studies used hospitalization rates as proxy for severity.

Methods: We evaluated data from coronavirus disease 2019 (COVID-19) cases diagnosed in French pwCF followed in one of the 47 French CF center over the first year of the pandemic.

Objective: criteria were applied for defining severity (e.g., respiratory failure and/or death). Data were compared to those from all French pwCF using the French CF Registry.

Results: As of April 30, 2021, 223 pwCF were diagnosed with COVID-19, with higher risks in adults (≥ 18 years, odds ratio [OR] = 2.52, 95% confidence interval [CI] = 1.82-3.48) and post-transplant individuals (OR = 2.68, 95% CI = 1.98-3.63). Sixty (26.9%) patients were hospitalized, with an increased risk in post-transplant individuals (OR = 4.74, 95% CI = 2.49-9.02). In 34 (15%) cases, COVID-19 was considered severe; 28/60 (46.7%) hospitalizations occurred in patients without objective criteria of severity. Severe cases occurred mostly in adults (85.3%) and post-transplant pwCF (61.8%, OR = 6.02, 95% CI = 2.77-13.06). In non-transplanted pwCF, risk factors for severity included low lung function (median ppFEV1 54.6% vs. 75.1%, OR = 1.04, 95% CI = 1.01-1.08) and CF-associated diabetes (OR = 3.26, 95% CI = 1.02-10.4). While most cases recovered without sequelae ($n = 204$, 91.5%), 16 (13%) were followed for possible sequelae, and three post-transplant females died.

Conclusions: Severe COVID-19 cases occurred infrequently during the first year of the pandemic in French pwCF. Non-transplanted adults with severe respiratory disease or diabetes and post-transplant individuals were at risk for severe COVID-19. Thus, specific preventive measures should be proposed."

Clin Infect Dis: [Impact of Vaccination and Early Monoclonal Antibody Therapy on COVID-19 Outcomes in Organ Transplant Recipients During the Omicron Wave](#) [Get access Arrow](#) (21 April 2022)

"Background: Solid organ transplant (SOT) recipients are at high risk for complications from COVID-19 and vaccine breakthrough infections are common. We determined the effectiveness of ≥ 3 doses of mRNA vaccine and early monoclonal antibody therapy in reducing disease severity against the Omicron (B.1.1.529) variant.

Methods: Prospective cohort study of consecutive SOT recipients with SARS-CoV-2 infection referred to our transplant center who were followed for at least 30 days. The primary

outcome was supplemental oxygen requirement. Effectiveness of sotrovimab and ≥ 3 vaccine doses was estimated using adjusted risk ratios (RR).

Results: Three-hundred adult organ transplant recipients were included. Seventy-one patients (24.1%) were hospitalized, 44(14.9%) required supplemental oxygen, 19(6.5%) were admitted to the ICU, 15(5.1%) required MV, and 13(4.4%) died. On multivariate analysis, age and multiple comorbidities were risk factors for oxygen requirement. Both receipt of ≥ 3 vaccine doses prior to SARS-CoV-2 infection and receipt of sotrovimab in the first 7 days of symptom onset was associated with a reduction in the need for supplemental oxygen [RR 0.30 (95%CI:0.17 to 0.54) and RR 0.24 (95% CI:0.1 to 0.59) respectively]. For sotrovimab, the number needed to treat (NNT) to prevent one patient requiring oxygen was 6.64 (95%CI:4.56-13.66). Both sotrovimab use and having received ≥ 3 vaccine doses were also associated with a shorter hospitalization length of stay.

Conclusion: In a cohort of SOT recipients with Omicron variant COVID-19 infection, prior receipt of ≥ 3 mRNA vaccine doses and early monoclonal antibody therapy were independently associated with significantly reduced disease severity."

JAMA Oncol: [Evaluation of the Durability of the Immune Humoral Response to COVID-19 Vaccines in Patients With Cancer Undergoing Treatment or Who Received a Stem Cell Transplant](#) (21 April 2022)

"Question: What is the durability of the antibody response to COVID-19 vaccines in patients with cancer undergoing treatment or who received a stem cell transplant?

Findings: In this cross-sectional study of 453 patients with cancer undergoing treatment or who received a stem cell transplant, the geometric mean titers for the anti-SARS-CoV-2 spike protein receptor binding domain were 470.38 U/mL 1 month after the second dose of the vaccine, 447.23 U/mL 6 months after the second dose, and 9224.85 U/mL 1 month after a third dose.

Meaning: This study suggests that for patients with cancer undergoing treatment or who received a stem cell transplant, antibody titers peak 1 month after the second dose of a messenger RNA vaccine and are sustained over 6 months; compared with the primary vaccine course, a 20-fold increase in geometric mean titers after a third suggests a robust B-cell response."

Long COVID and Other Post-Infectious Findings

News in Brief

"The case for testing Pfizer's Paxlovid for treating long COVID" ([Reuters](#)).

Long Reads

"She went to one doctor, then another and another: Lindsay Polega's two-year odyssey with long covid shows how the medical system fails many patients" ([WP](#)).

Journal Articles

Clin Infect Dis: [Multisystem inflammatory syndrome in adults \(MIS-A\): case finding through systematic review of electronic medical records](#) (20 April 2022)

"Background: Multisystem inflammatory syndrome in adults (MIS-A) is a severe condition temporally associated with SARS-CoV-2 infection.

Methods: In this retrospective cohort study, we applied the U.S. Centers for Disease Control and Prevention (CDC) case definition to identify diagnosed and undiagnosed MIS-A cases among adults discharged April 2020-January 2021 from four Atlanta, Georgia hospitals affiliated with a single medical center. Non-MIS-A COVID-19 hospitalizations were identified using International Classification of Diseases, Tenth Revision encounter code U07.1. We calculated the ratio of MIS-A to COVID-19 hospitalizations, compared demographic characteristics of the two cohorts, and described clinical characteristics of MIS-A patients.

Results: We identified 11 MIS-A cases, none of which were diagnosed by the treatment team, and 5,755 COVID-19 hospitalizations (ratio 1: 523). Compared with patients with COVID-19, patients with MIS-A were more likely to be younger than 50 years (72.7% vs. 26.1%, $p < 0.01$) and to be non-Hispanic Black persons (81.8% vs. 50.0%, $p = 0.04$). Ten patients with MIS-A (90.9%) had at least one underlying medical condition. Two MIS-A patients (18.2%) had a previous episode of laboratory-confirmed COVID-19, occurring 37 and 55 days prior to admission. All MIS-A patients developed left ventricular systolic dysfunction. None had documented mucocutaneous involvement. All required intensive care, all received systemic corticosteroids, eight (72.7%) required mechanical ventilation, two (18.2%) required mechanical cardiovascular circulatory support, and none received intravenous immunoglobulin. Two (18.2%) died or were discharged to hospice.

Conclusions: MIS-A is severe but likely underrecognized complication of SARS-CoV-2 infection. Improved recognition of MIS-A is needed to quantify its burden and identify populations at highest risk."

J Infect Dis: [Global Prevalence of Post COVID-19 Condition or Long COVID: A Meta-Analysis and Systematic Review](#) (16 April 2022)

"Introduction: This study aims to examine the worldwide prevalence of post COVID-19 condition, through a systematic review and meta-analysis.

Methods: PubMed, Embase, and iSearch were searched on July 5, 2021 with verification extending to March 13, 2022. Using a random effects framework with DerSimonian-Laird estimator, we meta-analyzed post COVID-19 condition prevalence at 28+ days from infection.

Results: 50 studies were included, and 41 were meta-analyzed. Global estimated pooled prevalence of post COVID-19 condition was 0.43 (95% CI: 0.39,0.46). Hospitalized and non-hospitalized patients have estimates of 0.54 (95% CI: 0.44,0.63) and 0.34 (95% CI: 0.25,0.46), respectively. Regional prevalence estimates were Asia- 0.51 (95% CI: 0.37,0.65), Europe- 0.44 (95% CI: 0.32,0.56), and North America- 0.31 (95% CI: 0.21,0.43). Global prevalence for 30, 60, 90, and 120 days after infection were estimated to be 0.37 (95% CI: 0.26,0.49), 0.25 (95% CI: 0.15,0.38), 0.32 (95% CI: 0.14,0.57) and 0.49 (95% CI: 0.40,0.59), respectively. Fatigue was the most common symptom reported with a prevalence of 0.23 (95% CI: 0.17,0.30), followed by memory problems (0.14 [95% CI: 0.10,0.19]).

Discussion: This study finds post COVID-19 condition prevalence is substantial; the health effects of COVID-19 appear to be prolonged and can exert stress on the healthcare system."

Pregnancy and Postpartum Period

News in Brief

"Pregnant women with COVID-19 face greater risk of hospitalisation and ICU admission, strengthening case for vaccination: Findings suggest women with COVID-19 during pregnancy are five times more likely to be hospitalised, and six times as likely to require treatment in intensive care" ([EurekAlert](#); see also: [ECCMID abstract \[google drive pdf\]](#)).

Journal Articles

JAMA: [Receipt of COVID-19 Booster Dose Among Fully Vaccinated Pregnant Individuals Aged 18 to 49 Years by Key Demographics](#) (22 April 2022)

"This study uses data from the Vaccine Safety Datalink on receipt of booster doses of COVID-19 vaccines among pregnant individuals aged 18 to 49 years....

Using data from the VSD, it is estimated that less than half of fully vaccinated pregnant individuals had received a COVID-19 booster dose by February 2022 with differences observed by age and race and ethnicity."

JAMA Netw Open: [Fresh Embryo Transfer Cycle Characteristics and Outcomes Following In Vitro Fertilization via Intracytoplasmic Sperm Injection Among Patients With and Without COVID-19 Vaccination](#) (22 April 2022)

"This cohort study examines the association of COVID-19 vaccination status and in vitro fertilization (IVF)-fresh embryo transfer cycle stimulation characteristics and outcomes....

To our knowledge, this is one of the first studies to evaluate the association of COVID-19 vaccination status with IVF-fresh embryo transfer cycles (including a high proportion of standard insemination cycles). We found no evidence to suggest that COVID-19 vaccination negatively affects cycle stimulation characteristics, embryological variables, or clinical outcomes in IVF. Current and emerging scientific evidence continues to support that COVID-19 vaccination is safe and effective and has no impact on fertility. The results of this study can be used to provide reassuring data to patients planning on pregnancy considering COVID-19 vaccination."

Pediatric Population

News in Brief

"Pfizer asks FDA to authorize booster shots for kids ages 5 through 11" ([NPR](#)).

"Moderna files for U.S. authorization of COVID shot for kids under 6" ([Reuters](#)).

"FDA approves first COVID-19 treatment [remdesivir] for young children" ([FDA](#)).

Beyond COVID

"Health authorities in North Carolina say they are investigating two cases of hepatitis in young children, making the state the second to report cases that appear to be linked [to an outbreak](#) that is being seen in a growing number of countries" ([STAT](#); see also: [CDC Health Advisory \[pdf\]](#), [UK Health Security Agency story](#), and [ECDC update](#)).

"A new puberty guide for kids aims to replace anxiety with self-confidence" ([NPR](#)).

Journal Articles

JAMA Pediatr: [Association of Social Determinants of Health and Vaccinations With Child Mental Health During the COVID-19 Pandemic in the US](#) (27 April 2022)

"Question: To what extent are individual and structural social determinants of health (SDoH) and vaccinations associated with child mental health during the COVID-19 pandemic?

Findings: In this cohort study of 8493 US children, pandemic-related food insecurity, parental unemployment, disrupted mental health treatment, living in neighborhoods with higher shares of adults working full-time, and living in states lagging in vaccination rates were associated with increased trajectories of perceived stress, sadness, and COVID-19–related worry. Associations between SDoH and these mental health outcomes were more common among Asian, Black, and Hispanic children more than White children.

Meaning: Supporting children’s mental health requires multifaceted policies that address SDoH and structural barriers to food, health services, employment protection, and vaccination."

JAMA Pediatr: [Evaluation of Suicides Among US Adolescents During the COVID-19 Pandemic](#) (25 April 2022)

"This cross-sectional study examines the pattern of suicides from 2015 through 2020 among youth aged 10 to 19 years in 14 US states....

Georgia, Indiana, New Jersey, Oklahoma, and Virginia had an increase in absolute count of adolescent suicides during the pandemic. These states, along with California, also had an increase in the proportion of overall suicides among adolescents. In contrast, Montana had a decrease in both absolute count and proportion of adolescent suicides during the pandemic, whereas Alaska had a decrease in proportion only. When data were aggregated across all 14 states, the proportion of overall suicides among adolescents increased during the pandemic. No other pandemic-period changes in adolescent outcomes were statistically significant."

MMWR: [Hospitalizations of Children Aged 5–11 Years with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, March 2020–February 2022](#) (22 April 2022)

"What is already known about this topic? State immunization programs conduct annual kindergarten vaccination assessments to monitor school entry vaccination coverage with all state-required vaccines.

What is added by this report? For the 2020–21 school year, coverage was approximately 94% for all required vaccines, approximately one percentage point lower than the previous school year. The exemption rate remained low at 2.2%.

What are the implications for public health practice? Disruptions caused by COVID-19 reduced reported enrollment, school response rates, and documentation for the 2020–21 school year. Schools and immunization programs can increase follow-up with undervaccinated students to reduce the impact of COVID-19–associated disruptions on vaccination coverage to protect students during the return to in-person learning."



MMWR: [Vaccination Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2020–21 School Year](#) (22 April 2022)

"What is already known about this topic? State immunization programs conduct annual kindergarten vaccination assessments to monitor school entry vaccination coverage with all state-required vaccines.

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Clin Infect Dis: [Neutralization of SARS-CoV-2 Omicron and other variants in serum from children with vaccination-induced myocarditis](#) (21 April 2022)

"Our study demonstrates that children who developed SARS-CoV-2 vaccination-induced myocarditis and may not receive another vaccination, could be susceptible to infection with Omicron and emerging variants. We observed higher neutralizing antibody titers in myocarditis patients vs. healthy vaccinated children, but significantly lower neutralization titers against Omicron in both groups."

JAMA Pediatr: [Acute Upper Airway Disease in Children With the Omicron \(B.1.1.529\) Variant of SARS-CoV-2-A Report From the US National COVID Cohort Collaborative](#) (15 April 2022)

"This cohort study uses data from the US National COVID Cohort Collaborative to evaluate upper airway infections in children during the surge of the Omicron (B.1.1.529) variant of SARS-CoV-2 in the US....

SARS-CoV-2–positive pediatric UAI rates increased during the Omicron surge. More than one-fifth of children hospitalized with SARS-CoV-2 and UAI developed severe disease. Given the high proportion of UAI cases during the Omicron period, these results appear to support recent mechanistic reports."

Biomolecules: [Long COVID-19 in Children: From the Pathogenesis to the Biologically Plausible Roots of the Syndrome](#) (08 April 2022)

"Long Coronavirus disease-19 (COVID-19) refers to the persistence of symptoms related to the infection with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). This condition is described as persistent and can manifest in various combinations of signs and symptoms, such as fatigue, headache, dyspnea, depression, cognitive impairment, and altered perception of smells and tastes. Long COVID-19 may be due to long-term damage to different organs-such as lung, brain, kidney, and heart-caused by persisting viral-induced inflammation, immune dysregulation, autoimmunity, diffuse endothelial damage, and micro thrombosis. In this review, we discuss the potential and biologically plausible role of some vitamins, essential elements, and functional foods based on the hypothesis that an individual's dietary status may play an important adjunctive role in protective immunity against COVID-19 and possibly against its long-term consequences."

Pediatr Ann: [The Effect of COVID-19 on the Mental Health of Military Connected Children and Adolescents](#) (01 April 2022)

"With a growing body of literature describing the coronavirus disease 2019 (COVID-19) pandemic's effect on children and adolescents, there remain few official reports regarding mental health in military connected youth. With sparse literature available specifically in youth associated with the Armed Forces, published studies on global child and adolescent mental health during the COVID-19 pandemic are first reviewed. Military connected youth

have unique needs and experiences. Implications of pandemic-related stressors on their mental health are suggested based on analysis of disaster and deployment literature. Military members have continued to move and deploy throughout the pandemic. Uniformed families have high risk factors for mental health concerns. Managing the mental health of military connected youth will fall heavily on civilian providers, both in primary and subspecialty practices. As such, vigilance for psychological health concerns and familiarity with military resources are vital for the mental wellness of our military pediatric patients."

Healthcare Workers

Journal Articles

Mil Med: [Joining the Navy to Become a Physician: The Typical Experience](#) (27 April 2022)

"Introduction: The decision to enter the Navy as a physician is a major career choice. However, there are no published studies that address the typical Navy physician's experience in the Health Professions Scholarship Program (HPSP) and Uniformed Services University of the Health Sciences (USUHS) programs. The purpose of this qualitative study is to describe the typical Navy physician's experience in the HPSP and USUHS programs.

Materials and methods: An anonymous online survey containing 47 questions was distributed to 63 Navy HPSP and USUHS physicians who started internships from 2008 to 2015. Participants were chosen by using purposeful, criterion, and snowball sampling methods with whom the author had a professional relationship during his military experience. The survey data were plotted in Excel spreadsheets and graphs according to six sub-research questions. Mean, SD, Likert scale 1-5, and grouping of free text responses were recorded.

Results: A total of 54 out of 63 Navy physicians (85.7%) responded to the survey. Navy physicians got their first-choice residency selection of 67.3% of the time, 34.6% went straight through residency without interruptions, 44.2% answered definitely or probably that military match changed their residency selection compared to them applying for civilian residency, and 46.2% answered definitely or probably that it was more difficult to get into military versus civilian residency. Participants answered definitely or probably that military experience puts them ahead of civilians in terms of leadership (82.7%), prior medical experience (46.2%), and applying for civilian residency (76.2%). Common positive themes of free-text answers included having financial stability, unique life experiences, and serving their country. Common negative themes included lack of career control, lack of knowledge regarding HPSP/USUHS programs, and delay in residency and career.

Conclusions: The principal findings in this study are that most Navy physicians favored paid medical school/financial support, working overseas and in unique operational climates, having unique life experiences, leadership skills, and prior military experience put them ahead of their civilian colleagues, thought the Navy experience was worth it, and would join again if given the opportunity. However, most Navy physicians had a lack of career control due to needs of the Navy, lack of knowledge regarding residency selection, operational billets, and active duty service obligation, had more difficulty getting into a military residency of their choice versus civilians, and had interrupted residency training/training delays. The Navy would possibly benefit from a nationwide HPSP/USUHS physician mentorship program and an educational seminar to increase medical student applicant knowledge, which may improve recruiting and retention."

See also: Commentary: [Joining the Navy to Become a Physician: Nothing Typical About It](#)

Open Forum Infect Dis: [SARS-CoV-2 mRNA vaccine effectiveness in healthcare workers by dosing interval and time since vaccination: test negative design, British Columbia, Canada](#) (15 April 2022)

"Background: One- and two-dose mRNA vaccine effectiveness (VE) estimates against SARS-CoV-2 infection by dosing interval and time since vaccination were assessed among healthcare workers (HCWs) in publicly-funded acute and community (non-residential) healthcare facilities in British Columbia, Canada.

Methods: A test-negative design was used with (6:1) controls matched to cases on epidemiological week of SARS-CoV-2 test date. mRNA vaccination was defined by receipt of the first dose ≥ 21 days or second dose ≥ 14 days before test date. HCWs ≥ 18 years old tested for SARS-CoV-2 between epi-weeks 3-39 (January 17-October 2, 2021) were included, when varying dosing intervals and a mix of circulating variants-of-concern contributed, including Delta dominance provincially from epi-week 31 (August 1).

Results: Single- and two-dose analyses included 1,265 and 1,246 cases, respectively. Median follow-up period was 49 days (interquartile range: 34-69) for single-dose and 89 days (interquartile range: 61-123) for two-dose recipients, with 12%, 31% and 58% of second doses given 3-5, 6 or ≥ 7 weeks after the first. Adjusted mRNA VE against SARS-CoV-2 was 71% [95% CI: 66, 76] for one dose and 90% [95% CI: 88, 92] for two doses, similar with two heterologous mRNA doses (92%; [95% CI: 86, 95]). Two-dose VE remained $>80\%$ at ≥ 28 weeks post-second dose. Two-dose VE was consistently 5-7% higher with ≥ 7 -week versus 3-5-week interval between doses.

Conclusions: In a HCW population, we report substantial single-dose and strong and sustained two-dose mRNA vaccine protection, the latter maintained at least seven months. Findings inform longer interval between doses, with global health and equity implications."

Mental Health and Wellness

News in Brief

"Even when the pandemic fades, the depression it has wrought will linger" ([STAT](#)).

Journal Articles

JAMA Intern Med: [Stress-Related Disorders of Family Members of Patients Admitted to the Intensive Care Unit With COVID-19](#) (25 April 2022)

"Question: What are the psychological sequelae of having a family member with COVID-19 admitted to the intensive care unit (ICU)?

Findings: In this prospective, mixed-methods cohort study of 330 family members of patients admitted to the ICU with COVID-19, family members had significant symptoms of posttraumatic stress disorder (PTSD) 3 months after the patients' admission to the ICU; higher PTSD symptoms scores were significantly associated with Hispanic ethnicity, female gender, and previous medication use for a psychiatric condition. Family members with higher scores more commonly described feelings of distrust and concern about the need to take clinicians' information at face value without being present to see for themselves.

Meaning: Having a family member with COVID-19 in the ICU was associated with a high prevalence of symptoms of PTSD, and identified associations may guide future interventions."

Lancet Public Health: [Policy stringency and mental health during the COVID-19 pandemic: a longitudinal analysis of data from 15 countries](#) (21 April 2022)

"Background: To date, public health policies implemented during the COVID-19 pandemic have been evaluated on the basis of their ability to reduce transmission and minimise economic harm. We aimed to assess the association between COVID-19 policy restrictions and mental health during the COVID-19 pandemic.

Methods: In this longitudinal analysis, we combined daily policy stringency data from the Oxford COVID-19 Government Response Tracker with psychological distress scores and life evaluations captured in the Imperial College London-YouGov COVID-19 Behaviour Tracker Global Survey in fortnightly cross-sections from samples of 15 countries between April 27, 2020, and June 28, 2021. The mental health questions provided a sample size of 432 642 valid responses, with an average of 14 918 responses every 2 weeks. To investigate how policy stringency was associated with mental health, we considered two potential mediators: observed physical distancing and perceptions of the government's handling of the pandemic. Countries were grouped on the basis of their response to the COVID-19

pandemic as those pursuing an elimination strategy (countries that aimed to eliminate community transmission of SARS-CoV-2 within their borders) or those pursuing a mitigation strategy (countries that aimed to control SARS-CoV-2 transmission). Using a combined dataset of country-level and individual-level data, we estimated linear regression models with country-fixed effects (ie, dummy variables representing the countries in our sample) and with individual and contextual covariates. Additionally, we analysed data from a sample of Nordic countries, to compare Sweden (that pursued a mitigation strategy) to other Nordic countries (that adopted a near-elimination strategy).

Findings: Controlling for individual and contextual variables, higher policy stringency was associated with higher mean psychological distress scores and lower life evaluations (standardised coefficients $\beta=0.014$ [95% CI 0.005 to 0.023] for psychological distress; $\beta=-0.010$ [-0.015 to -0.004] for life evaluation). Pandemic intensity (number of deaths per 100 000 inhabitants) was also associated with higher mean psychological distress scores and lower life evaluations (standardised coefficients $\beta=0.016$ [0.008 to 0.025] for psychological distress; $\beta=-0.010$ [-0.017 to -0.004] for life evaluation). The negative association between policy stringency and mental health was mediated by observed physical distancing and perceptions of the government's handling of the pandemic. We observed that countries pursuing an elimination strategy used different policy timings and intensities compared with countries pursuing a mitigation strategy. The containment policies of countries pursuing elimination strategies were on average less stringent, and fewer deaths were observed.

Interpretation: Changes in mental health measures during the first 15 months of the COVID-19 pandemic were small. More stringent COVID-19 policies were associated with poorer mental health. Elimination strategies minimised transmission and deaths, while restricting mental health effects."

Other Infectious Diseases and Public Health Threats

News in Brief

"U.S. case of human avian influenza A(H5) virus reported" ([CDC](#)).

"USDA confirms highly pathogenic avian influenza in Idaho" ([USDA](#)).

"New Ebola outbreak declared in DRC after single case confirmed" ([CNN](#)).

"Biotech firm announces results from first US trial of genetically modified mosquitoes" ([Nature](#)).

"A tick bite made them allergic to meat — and an organ-transplant company has an unexpected solution" ([Atlantic](#)).

"Drug-resistant fungus could be spreading from the environment to the clinic" ([CIDRAP](#); see also: [Nature Microbiology paper](#)).

Vaccines

"Covid vaccine concerns are starting to spill over into routine immunizations: Public health leaders fear preventable and possibly fatal diseases could become more common" ([Politico](#)).

"Initial results from Novavax' COVID-19-Influenza vaccine trial are first to show feasibility of combination vaccine" ([Novavax](#)).

April 25th is World Malaria Day: "Over 1 million African children protected by first malaria vaccine" ([WHO](#)).

"Vaccine-derived polio is on the rise. A new vaccine aims to stop the spread" ([NPR](#)).

Climate Change

"We created the 'Pandemicene': By completely rewiring the network of animal viruses, climate change is creating a new age of infectious dangers" ([Atlantic](#)).

"How climate change could drive animal movements — and threaten more viral spillovers" ([STAT](#); see also: [Nature study](#)).

Journal Articles

MMWR: [Public Health Actions to Control Measles Among Afghan Evacuees During Operation Allies Welcome — United States, September–November 2021](#) (29 April 2022)

"What is already known about this topic? Low measles immunization coverage and an ongoing measles outbreak in Afghanistan led to U.S. measles importations among Afghan evacuees who were resettled as part of Operation Allies Welcome.

What is added by this report? Forty-seven measles cases were reported among 72,299 Afghan evacuees (attack rate = 0.065%) in U.S. military bases and a contracted hotel. A coordinated response and a high-coverage mass vaccination campaign led to rapid containment.

What are the implications for public health practice? Mass vaccination of an undervaccinated evacuee population can limit measles importations, control measles spread, and prevent transmission into U.S. communities."

See also: [Notes from the Field: Response to Measles Among Persons Evacuated from Afghanistan — Joint Base McGuire-Dix-Lakehurst, New Jersey, August–October 2021](#)

Euro Surveill: [Clostridioides difficile positivity rate and PCR ribotype distribution on retail potatoes in 12 European countries, January to June 2018](#) (14 April 2022)

"Background: While human-to-human transmission of *Clostridioides difficile* occurs often, other infection sources, including food, animals and environment, are under investigation.

Aim: We present a large study on *C. difficile* in a food item in Europe, encompassing 12 European countries (Austria, France, Greece, Ireland, Italy, the Netherlands, Poland, Slovakia, Spain, Sweden, Romania and the United Kingdom).

Methods: Potato was selected because of availability, ease of sampling and high *C. difficile* positivity rates. Identical protocols for sampling and isolation were used, enabling a direct comparison of the *C. difficile* positivity rate.

Results: From *C. difficile*-positive potato samples (33/147; 22.4%), we obtained 504 isolates, grouped into 38 PCR ribotypes. Positivity rates per country varied (0-100%) and were at least 10% in 9/12 countries. No geographical clustering of samples with high positivity rates or in PCR ribotype distribution was observed. The most frequently detected PCR ribotypes (014/020, 078/126, 010 and 023) are also commonly reported in Europe among human clinically relevant isolates, in animal isolates and in the environment. Whole genome sequencing revealed several genetically related strain pairs (Spain/RT126, France/RT010, Austria and Sweden/RT276) and a cluster of very similar strains in RT078/126.

Conclusion: Our results suggest, the high potato contamination rates could have public health relevance. They indicate potatoes can serve as a vector for introducing *C. difficile* spores in the household environment, where the bacterium can then multiply in sensitive hosts with disrupted or immature microbiota. Potato contamination with PCR ribotypes shared between humans, animals and soil is supportive of this view."

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